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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,323	09/01/2000	Michael R. Hayden	50110/004002	5878

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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,323	HAYDEN ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51,57-84 and 92-94* is/are pending in the application.

4a) Of the above claim(s) *1-49,57-79 and 92-94* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50,51 and 80-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

[1] Claims 1-51, 57-84, and 92-94 are pending in the application.

[2] Applicants' amendment filed September 22, 2003, is acknowledged. This amendment replaces all previous versions and listings of the claims in the instant application.

[3] Claims 1-49, 57-79, and 92-94 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

[4] Claims 50-51 and 80-84 are being examined on the merits.

[5] Applicants' arguments filed September 22, 2003 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[6] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Information Disclosure Statement

[7] Applicants' remarks regarding two additional IDSs filed December 4, 2000 and July 29, 2002 are acknowledged. While the examiner has located the IDS filed December 4, 2000, the IDS allegedly filed July 29, 2002 cannot be located. Applicants are requested to re-submit this IDS.

Election/Restriction

[8] Applicants' election with traverse of Group I, claims 50-51 and 80-84, drawn to a method for determining a propensity for developing a disease or condition by detecting a Q597R polymorphism relative to SEQ ID NO:2 in the amendment filed September 22, 2003, is acknowledged. Applicants traverse the instant restriction requirement by arguing that the claims can be searched without reference to a particular sequence as a search of claim 50 must begin with the generic aspects of the claim. Applicants' argument is not found persuasive.

It is noted that, as written, claim 50 requires a sequence search as SEQ ID NO:2 is recited as a reference sequence to which other sequences would be compared in order to identify a polymorphism. Even if the claim did not recite "SEQ ID NO:2" as a limitation, in order to perform a complete search, the examiner would necessarily be required to search SEQ ID NO:2. Absent a search of SEQ ID NO:2, the search would not be complete as it is possible the generic terms recited in the claims would not be used in a prior art reference that nonetheless anticipates or renders obvious the claimed invention. Furthermore, a sequence search is useful in narrowing the search hits and is additionally useful in identifying applications that claim the same invention as the instant application that may otherwise go unnoticed.

Applicants argue claim 50 rests on a relationship between ABCA1 protein and cardiovascular disease, which relationship was allegedly first identified by applicants. Applicants argue that because they were allegedly the first to identify this relationship,

searching sequences is irrelevant. Applicants argue that even if a polymorphism in SEQ ID NO:2 were reported in the prior art, it would be irrelevant to claim 50 as this claim requires determining a risk of cardiovascular disease, which applicants allege, no one would have done because this allegedly was not known prior to applicants' teaching. Applicants' argument is not found persuasive.

To the extent the claims are drawn to the elected invention, *i.e.,* a method for determining a propensity for developing a disease or condition by detecting a Q597R polymorphism relative to SEQ ID NO:2 in an ABC1 protein, the claimed invention appears to be novel in view of the prior art of record (see the discussion of the rejection under 102(b) below). However, regarding applicants' argument that they are the first to identify a relationship between ABC1 and cardiovascular disease, it is noted that the references of Rust et al. and Bodzioch et al. (already of record), which were published prior to the effective filing date of the instant application, teach mutations in an ABC1 polypeptide that result in lower HDL levels that are indicative of developing cardiovascular disease (see items 12 and 13 of the Office action mailed October 22, 2002). In this regard, a sequence search aids in distinguishing between the ABC1 polymorphisms identified by Rust et al. and Bodzioch et. and any other ABC1 polymorphisms that may have been identified and reported in the prior art. Furthermore, it is noted that the numbering of amino acids and nucleotides of a given sequence are often used inconsistently in the prior art and thus, the same polymorphism may be identified by a different amino acid/nucleotide number. A sequence search enables the

examiner to search for polymorphisms independent of amino acid/nucleotide numbering.

Applicants argue that limitation of the invention to a particular polymorphism or set of polymorphisms would unduly limit the breadth of the protected invention. Applicants argue that the determination of a polymorphism is a routine matter. Applicants argue the disclosed polymorphisms are intended to support the invention and not limit it and if the effect of other polymorphisms is to be evaluated, the specification discloses a simple activity assay. Applicants' argument is not found persuasive.

The issue at hand is whether the examiner properly restricted the claims according to 35 USC 121. The examiner has restricted the claims to a method for identifying a particular polymorphism or set of polymorphisms (see the Office action mailed June 19, 2003). MPEP § 803 sets forth two criteria for a proper restriction between patentably distinct inventions: (A) The inventions must be independent or distinct as claimed and (B) There must be a serious burden on the examiner. Each of the methods of inventions I-XII is patentably distinct as each recited polymorphism or set of polymorphisms of SEQ ID NO:2 represents a structurally distinct polypeptide sequence and thus, the methods of inventions I-XII are independent as they utilize different products. That the methods of inventions I-XII are independent is undisputed by applicants. This satisfies the first criterion for restriction. As each of the polymorphisms identified by Groups I-XII requires a different search (that is required for the search to be complete as described in detail above), the second criterion for

restriction is satisfied. Thus, the examiner properly restricted the claims according to 35 USC 121.

Applicants suggest that, if a generic claim is not found allowable, an interview should be arranged. Applicants assert that their election should be interpreted by the examiner as an election of species for examination purposes and not an election of an invention.

Applicants' suggestion for interview is noted. However, in order for the examiner to draft and submit the instant Office action in a timely manner (due to Office imposed deadlines), an interview could not be arranged prior to drafting and submitting the instant Office action. However, if applicants desire to schedule an interview following receipt of the instant Office action, applicants are invited to contact the examiner at the telephone number provided at the end of this Office action.

Also, applicants' assertion that the election be made as an election of species is also noted. However, the election has been interpreted as an election of invention for the reasons that follow. MPEP § 803.02 states, "[i]f the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions". As stated above, each of the polymorphic sequences is distinct in structure, requiring a separate search. Therefore, co-examination of all polymorphic sequences encompassed by the claims would place a serious burden on the examiner. Even assuming *arguendo* that a search for the claims

did not place a serious burden on the examiner, it is noted that MPEP § 803.02 further states, "it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention" and "[b]roadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility". While the claimed inventions (inventions I-XII) all share a common utility, *i.e.,* methods of determining an individual's predisposition to cardiovascular disease, the methods recite distinct polymorphisms that do not share a substantial structural feature that is essential to each invention's utility. Therefore, the election is not a species election, but is an election of invention, i.e., Invention I, claims 50-51 and 80-84, drawn to a method for determining a propensity for developing a disease or condition by detecting a Q597R polymorphism relative to SEQ ID NO:2.

[9] The subject matter of Inventions II-XII as set forth in the restriction requirement mailed June 19, 2003, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

[10] Claims 50-51 and 80-84 are being examined only to the extent the claims read on the elected subject matter.

Specification/Informalities

[11] The attempt to incorporate subject matter into this application by reference to a hyperlink embedded in the specification (for example, page 48, lines 5-6 and page 98,

line 2) is improper. Incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01 regarding hyperlinks in the specification and 608.01(p), paragraph I regarding incorporation by reference.

Claim Objections

[12] Claims 50-51 and 80-84 are objected to as reciting non-elected subject matter. It is suggested that, for example, applicants amend the claims to recite or depend from claims that recite the elected invention. The claims have been examined as though they recite a Q597R ABC1 polymorphism in accordance with the election of September 22, 2003.

Claim Rejections - 35 USC § 112, Second Paragraph

[13] In view of applicants' amendment to claims 50-51 and 82-84, the rejection under 35 U.S.C. § 112, second paragraph as set forth in items 5-9 of the Office action mailed October 22, 2002, is withdrawn.

[14] Claim(s) 50-51 and 80-84 is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated in view of applicants' election of the Invention of Group I to drawn to a method reciting the polymorphism of Q597R.

[a] Claim 50 (claims 51 and 80-84 dependent therefrom) is confusing as the claim recites "the amino acid sequence of SEQ ID NO:2". However, the latest paper copy of the sequence listing indicates that SEQ ID NO:2 is an oligonucleotide sequence. Based on the specification (see, *e.g.*, page 17, lines 15-16) that SEQ ID NO:5 is the amino acid sequence of ABCA1. In the interest of advancing prosecution, the claim has been interpreted as though it recited SEQ ID NO:5 instead of SEQ ID NO:2.

[b] Claims 50-51 and 80-84 are confusing. Figure 11 indicates that a Q597R mutation in SEQ ID NO:2 has "no CHD". The examiner can find no definition of the term "CHD" and has interpreted the term as "coronary heart disease". Thus, Figure 11 indicates that a Q597R mutation in ABCA1 is not indicative of a risk for cardiovascular disease as claim 50 would suggest. Applicants are invited to present evidence demonstrating a Q597R mutation in SEQ ID NO:5 is indicative of a predisposition to cardiovascular disease. It is suggested that applicants clarify the meaning of the claims.

[c] Claim 51 is confusing as the polymorphism is "present at more than one of the polymorphic sites shown in Figure 11". It is unclear as to how a Q597R polymorphism can be present at more than one of the polymorphic sites shown in Figure 11. It is suggested that applicants clarify the meaning of the claim.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

[15] Claims 50-51 and 80-84 are rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility. This rejection is necessitated by amendment. MPEP § 2107.01 states, "[a]n invention that is 'inoperative' (i.e., it does not operate to produce the results claimed by the patent applicant) is not a 'useful' invention in the meaning of the patent law". In this case, based on the information provided in Figure 11 as described above, it appears that a Q597R mutation in SEQ ID NO:5 is not indicative of risk for cardiovascular disease. In the absence of evidence demonstrating a Q597R mutation in SEQ ID NO:5 is indicative of a predisposition to cardiovascular disease, the claimed invention is deemed inoperative. Applicants are invited to present evidence demonstrating a Q597R mutation in SEQ ID NO:5 is indicative of a predisposition to cardiovascular disease.

Claim Rejections - 35 USC § 112, First Paragraph

[16] In view of applicants' election of the invention of Group I, drawn to a method of determining an individual's predisposition to cardiovascular disease by determining the presence or absence of a Q597R polymorphism, the written description rejection of claims 50-51 and 80-84 under 35 USC 112, first paragraph, as set forth in item 10 of the Office action mailed October 22, 2002, is withdrawn.

[17] In view of applicants' election of the invention of Group I, drawn to a method of determining an individual's predisposition to cardiovascular disease by determining the presence or absence of a Q597R polymorphism, the scope of enablement rejection of

clams 50-51 and 80-84 under 35 USC 112, first paragraph, as set forth in item 11 of the Office action mailed October 22, 2002, is withdrawn.

[18] Claims 50-51 and 80-84 are rejected under 35 U.S.C. 112, first paragraph. This rejection is necessitated by amendment. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 102

[19] In view of applicants' election of the invention of Group I, drawn to a method of determining an individual's predisposition to cardiovascular disease by determining the presence or absence of a Q597R polymorphism, the rejections of claims 50 and 80-82 under 35 USC 102(b) as being anticipated by Rust et al. and Bodzioch et al. are withdrawn. Rust et al. and Bodzioch et al. identify ABC1 mutations in individuals having Tangier Disease (see page 354, Figure 4 of Rust et al. and page 349, Figure 3 of Bodzioch et al.). However, neither Rust et al. nor Bodzioch et al. teach determining the presence of a Q597R polymorphism relative to SEQ ID NO:2 in individuals having Tangier Disease.

Conclusion

[20] Status of the claims:

- Claims 1-51, 57-84, and 92-94 are pending.

- Claims 1-49, 57-79, and 92-94 are withdrawn from consideration.
- Claims 50-51 and 80-84 are rejected.
- No claim is in condition for allowance.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652

Rebecca Prouty

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